Reaction of amidrazones with 1,4-diphenylbut-2-yne-1,4-dione

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Various (2*Z*)-2-({(*E*)[arylamino]phenylmethylene}hydrazono)-1,4-diphenylbutan-1,4-diones are obtained during the reaction of amidrazones with 1,4-diphenylbut-2-yne-1,4-dione (DBD) in boiling ethanol.

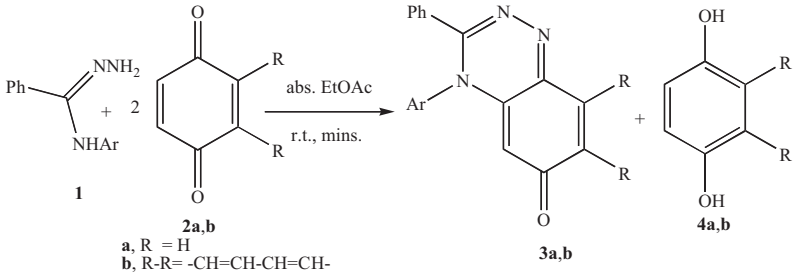
Keywords: amidrazones, 1,4-diphenylbut-2-yne-1,4-dione, imine formation

The chemistry of 1,4-diphenylbut-2-yne-1,4-dione (DBD) has been extensively investigated. For example, DBD reacts with benzimidazole-2-thione to produce 2-(acylvinylthio) benzimidazoles,[1] whilst diarylazines react with DBD to produce pyridazines *via* a Diels–Alder reaction.[2] An effective route to the pyrrol-2-ones involves the reaction of enamines with DBD.[3] Bis(phenylazo)stilbene undergoes facile cycloaddition with DBD to give 5,6-dibenzoyl-2,3a,4,6a-tetraphenyl-2,3a,4,6a-tetrahydro-1,2,3,4-tetraazapentalene.[4] DBD reacts with propane-1,3-dithiol in the presence of triphenylphosphine to afford the mesocyclic dithioether *trans*-2,3-dibenzoyl-1,4-dithiacycloheptane diastereoselectively.[5] Additionally, DBD reacts with enaminocarbonyl compounds to afford pyrrol-2-ol derivatives.[6] 2-Aryl thiocarbamoyl benzimidazolium salts derived from benzimidazole and imidazoline carbenes undergo cycloaddition reactions with DBD to furnish spiro(imidazole-2,3'-thiophenes).[7] Protonation of the highly reactive 1 : 1 intermediates produced in the reaction between alkyl isocyanides and DBD leads to vinylnitrilium cations, which undergo carbon-centred Michael type addition with the conjugate base of the NH-acid to produce highly functionalised aminofuran derivatives.[8] It is reported that amidrazones condense only with dicarbonyl compounds to yield 1,2,4-triazines.[9-11] The cyclocondensation reactions between amidrazones and ketoesters afford the corresponding triazinones.[12] Various naphtho[2,3-*f*][1,2,4]triazepine-6,11-diones have been obtained from the reaction of amidrazones with 1,4-dioxo-1,4-dihydronaphthalene-2,3-dicarbonitrile.[13] Amidrazones were also involved in the reaction with 2-(1,3-dioxo-indan-2-ylidene)malononitrile to produce the corresponding 1,2,4-triazoles.[14] Recently, we have investigated the reaction of 2,3-diphenylcyclopropenone with *N*-imidoyl-thioureas as amidine analogues. The reaction involves a stepwise addition and produces pyrimidin-4(3*H*)-ones.[15] Treatment of amidrazones with alkyl ketones under acidic catalysis leads generally to dihydro-1,2,4-triazoles.[16] The reaction of DBD with *N*,*N*′-substituted glyoxal-bisimines leads to the formation of pentasubstituted 1,2-dihydropyridines.[17] Aly *et al.* obtained various benzo- and naphtha[1,2,4]triazin-6(4*H*)-ones **3a**,**b** from the reaction of amidrazones **1** with benzo- and naphtho-1,4-quinones **2a**,**b** (Scheme 1).[18] To the best of our knowledge, there is no literature report of the reaction of amidrazones with π-deficient alkynes. In this paper, we report a new straightforward reaction of amidrazones with 1,4-diphenylbut-2-yne-1,4-dione.

Results and discussion

Amidrazones **1a–e** reacted with 1,4-diphenylbut-2-yne-1,4-dione (**5**) in absolute boiling ethanol, in 10–16 h, to produce, after chromatographic purification and recrystallisation, compounds **6a–e** in 70–94% yields (Scheme 2). We chose amidrazones **1a–e** having aryl groups with either electron-donating or -withdrawing substitutents on the benzene ring, in order to examine their effect on the reaction. Elemental analyses and IR, NMR (^{1}H and ^{13}C) and mass spectra were in good agreement with the assigned structures **6a–e** (Scheme 2).

For example, the IR spectrum of **6a** had two strong bands characteristic of the C=N at ν = 1610 and 1600, carbonyl at ν = 1700-1690, and an absorption band at ν = 3210 assigned to NH stretching. The elemental analysis and mass spectrum of **6a** proved its molecular formula as $C_{30}H_{25}N_3O_3$. The ^{1}H NMR spectrum of **6a** showed the presence of OCH_3, CH_2-benzoyl and NH-protons as three singlets at δ = 3.74, 4.76, and 8.24, respectively. The protons of the four aryl groups resonated as five multiplets at δ = 8.14–8.09 (2H), 7.58–7.52 (6H), 7.48–7.42 (2H), 7.38–7.27 (5H), 7.22–7.16 (2H), and in addition a doublet at δ = 6.67 (2H, *J* = 8.0 Hz). The ^{13}C NMR spectrum of **6a** revealed O*C*H$_3$ and *C*H$_2$-benzoyl at δ = 55.4 and 37.4, respectively. The two *C*=*N* carbon signals appeared at δ = 157.8 and 160.4, whereas the CH$_3$O-Ph *C* appeared at δ = 156.8 and the two carbonyl carbons resonated as two signals at δ = 193.3 and 196.1. The mass spectroscopy of **6a** indicated a peak at *m/z* = 248 (52%), whereas the molecular peak appeared at *m/z* = 475 (22%) as shown in Fig. 1. The base peak appeared at *m/z* = 105 corresponding to the PhCO$^{\cdot+}$ fragment. In the case of **6b**, the mass spectrum and elemental analysis established its molecular formula as $C_{29}H_{23}N_3O_2$. The ^{1}H NMR spectrum of **6b** showed seven multiplets for 20 aromatic protons at δ = 8.12–8.06 (2H), 8.04–8.00 (2H), 7.57–7.52 (2H), 7.48–7.32 (8H), 7.24–7.18 (2H), 7.16–7.12 (2H) and 7.04–6.92 (2H). The NH-proton absorbed clearly at δ = 8.16. The CH_2–benzoyl protons in **6b** resonated at δ = 4.70, whereas the *C*H$_2$-benzoyl carbon appeared in



Scheme 1 Reaction of amidrazones **1** with benzo- and naphtho-1,4-quinones **2a**,**b**.

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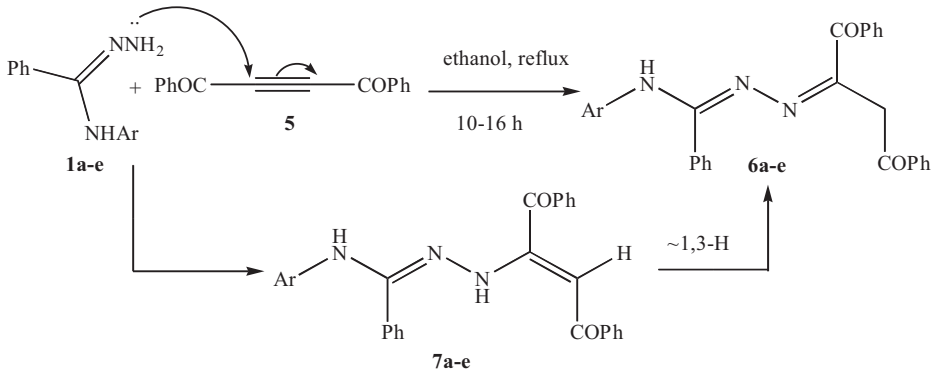

1, 6 and 7	Ar	Yield of 6 (%)
a	4-CH_3O-C_6H_4-	94
b	C_6H_5-	82
c	4-CH_3-C_6H_4-	88
d	4-Cl-C_6H_4-	75
e	3-Cl-C_6H_4-	70

Scheme 2 Reaction of amidrazones **1a-e** with DBD **5**.

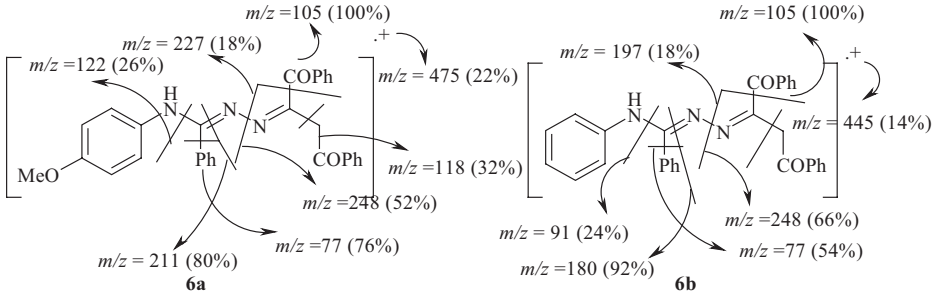

Fig. 1 Fragmentation patterns of mass spectroscopy for compounds **6a** and **6b**.

the ^{13}C NMR spectrum at δ = 37.4. The two *C=N* carbons resonated at δ = 158.2 and 159.8, whereas the two carbonyl carbons resonated at δ = 193.2 and 196.0. The mass spectral fragmentation patterns of **6a–e** (Fig. 1) are well in agreement with the assigned structures. Examples of the fragmentation patterns of compounds **6a** and **6b** are shown in Fig. 1.

The reaction can be described as due to nucleophilic addition of amidine-like addition on the acetylenic carbon to form the intermediate **7**, followed by 1,3-hydrogen shift to give **6** (Scheme 2). It is well-known that the equilibrium between imine N=C–CH_2 and enamine NH–C=CH can be shifted towards the enamine if the C=C is conjugated, or better yet part of an aromatic system. However, it was shown that imine is more stable than its enamine tautomer during the reaction of acetylene with primary amines.[19] In our case, it is reasonable that tautomerisation favours the imino form in the nitrogen system of **6a–e**. That simply is related to the conjugation system present in compounds **6a–e**, whereas this conjugation is obviously absent in the case of the isomeric forms **7a–e**. Since hydrazones have been demonstrated to possess, among other, antimicrobial, anticonvulsant, analgesic, antiinflammatory, antiplatelet, antitubercular and antitumoral activities,[20] we are aiming by this study to introduce prospective biological and/or pharmaceutical compounds.

Experimental

All melting points were recorded on a Gallenkamp apparatus. ^1H NMR and ^{13}C NMR spectra (Bruker AM 400, ^1H: 400.13 MHz, ^{13}C: 100.6 MHz). The NMR samples were dissolved in $CDCl_3$ solutions. Coupling constants were expressed in Hz. Elemental analyses were carried at the Assiut Microanalysis Centre of Assiut University. Mass spectroscopy was performed with a Finnigan MAT 8430 spectrometer at 70 eV, Institute of Organic Chemistry, Technical-University Braunschweig. IR spectra were run on a Shimadzu 470 spectrometer using KBr pellets.

Starting materials

Amidrazones **1a–e** and 1,4-diphenylbutyne-2-yne-1,4-dione (**5**) were prepared according to references 21 and 22, respectively.

General procedure

A 250 cm^3 two-necked round bottom flask containing a solution of **1a–e** (1 mmol) and **5** (1 mmol) in absolute ethanol (100 ml) was stirred at reflux for 10–16 h (the reaction was followed by TLC analysis). The solvent was then concentrated to its half volume and the precipitates were collected by filtration. The products **6a–e** were recrystallised from the stated solvents.

(2Z)-2-({(E)[4-Methoxyphenylamino]phenylmethylene}hydrazono)-1,4-diphenylbutan-1,4-dione **(6a):** Yellow crystals (0.45 g. 94%); R_f= 0.4 (CH_2Cl_2), m.p. 182°C (ethyl acetate). IR (KBr): ν = 3210 (m, NH), 3060–3010 (m, Ar–CH), 2990–2860 (m, aliph-CH), 1700–1690 (s, C=O), 1610, 1600 (s, C=N), 1598 (C=C) cm^{-1}. UV (CH_3CN): λ_{max} (log ε) = 410 (4.10). ^1H NMR ($CDCl_3$): δ = 8.24 (s, 1H, NH), 8.14–8.09 (m, 2H, ArH), 7.58–7.52 (m, 6H, ArH), 7.48–7.42 (m, 2H, ArH), 7.38–7.27 (m, 5H, ArH), 7.22–7.16 (m, 2H, ArH), 6.67 (d, 2H, *J* = 8.0 Hz, CH_3O–Ph-H), 4.76 (s, 2 H, CH_2-benzoyl), 3.74 (s, 3 H, OCH_3). ^{13}C NMR ($CDCl_3$): *δ* = 196.1, 193.3 (*C*O), 160.4, 157.8 (*C*=*N*), 156.8. (CH_3O-Ph *C*), 140.2 (*N*-Ph *C*), 138.6, 138.2, 136.2 (Ph *C*), 128.6, 128.0, 127.8, 127.6 (Ar *o*-2*C*H), 127.4, 127.2, 127.0 (Ar *m*-2CH), 126.8, 126.4, 126.2 (Ar *p*-*C*H), 114.1 (CH_3O-Ph 2*C*H), 55.4 (O*C*H_3), 37.4 (*C*H_2-benzoyl). MS (EI, 70 eV): *m/z* (%) = 475 [M^+] (22), 398 (20), 370 (24), 367 (22), 248 (52), 227 (18), 211 (80), 122 (26), 118 (32), 105 (100), 91 (26), 77 (76). $C_{30}H_{25}N_3O_3$ (475.55): Calcd. C, 75.77; H, 5.30; N, 8.84. Found: C, 75.70; H, 5.30; N, 8.74.

(2Z)-2-({(E}[Phenylamino]phenylmethylene}hydrazono)-1,4-diphenylbutan-1,4-dione **(6b):** Yellow crystals (0.36 g. 82%); R_f= 0.5 (CH_2Cl_2), m.p. 168°C (ethanol). - IR (KBr): ν = 3212 (m, NH), 3080-3010 (m, Ar-CH), 1706–1692 (s, C=O), 1612, 1604 (s, C=N), 1598 (m, C=C) cm^{-1}. UV (CH_3CN): λ_{max} (log ε) = 380 (4.00). ^1H NMR ($CDCl_3$): δ = 8.16 (s, 1H, NH), 8.12–8.06 (m, 2H, ArH), 8.04–8.00

(m, 2H, ArH), 7.57–7.52 (m, 2H, ArH), 7.48–7.32 (m, 8H, ArH), 7.24–7.18 (m, 2H, ArH), 7.16–7.12 (m, 2H, ArH), 7.04–6.92 (m, 2H, ArH), 4.70 (s, 2H, CH_2-benzoyl). ^{13}C NMR ($CDCl_3$): δ = 196.0, 193.2 (CO), 159.8, 158.2 (C=N), 140.0 (*N*-Ph *C*), 139.0, 138.8, 138.4 (Ph *C*), 128.6, 128.4, 128.0, 127.8 (Ar *o*-2*C*H), 127.6, 127.2, 127.0, 126.8 (Ar *m*-2*C*H), 126.6, 126.4, 126.2, 126.0 (Ar *p*-*C*H), 37.4 (*C*H_2-benzoyl). MS (EI, 70 eV): *m/z* (%) = 445 [M^+] (14), 248 (66), 197 (18), 180 (92), 118 (30), 91 (24), 105 (100), 77 (54). $C_{29}H_{23}N_3O_2$ (445.53): Calcd. C, 78.18; H, 5.20; N, 9.43. Found: C, 78.04; H, 5.30; N, 9.40.

(*2Z)-2-({(E}[4-Methylphenylamino]phenylmethylene}hydrazono)-1,4-diphenylbutan-1,4-dione* **(6c):** Yellow crystals (0.40 g. 88%); R_f = 0.45 (CH_2Cl_2), m.p. 196°C (methanol). IR (KBr): ν = 3210 (m, NH), 3065-3010 (m, Ar-CH), 2986–2870 (m, aliph-CH), 1708–1688 (C=O), 1610, 1600 (s, C=N), 1594 (s, C=C) cm^{-1}. UV (CH_3CN): λ_{max} (log ε) = 400 (4.06). ^1H NMR ($CDCl_3$): δ = 8.22 (s, 1H, NH), 8.15–8.06 (m, 2H, ArH), 7.60–7.50 (m, 4H, ArH), 7.40–7.25 (m, 7H, ArH), 7.22–7.10 (m, 4H, ArH), 7.04–6.92 (m, 2H, ArH), 4.70 (s, 2H, CH_2-benzoyl), 2.38 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ = 196.2, 193.0 (*C*O), 160.2, 157.5 (*C*=*N*), 140.0 (*N*-Ph *C*), 139.2, 138.2, 138.0, 137.6 (Ph *C*), 128.6, 128.0, 127.6, 127.0 (Ar *o*-2*C*H), 126.8, 126.6, 126.4, 126.2 (Ar *m*-2CH), 125.8, 125.4, 125.2 (Ar *p*-*C*H), 37.8 (*C*H_2-benzoyl), 32.8 (*C*H_3). MS (EI, 70 eV): *m/z* (%) = 459 [M^+] (24), 248 (60), 211 (24), 180 (80), 118 (34), 105 (100), 77 (50). $C_{30}H_{25}N_3O_2$ (459.55): Calcd. C, 78.41; H, 5.48; N, 9.14. Found: C, 78.60; H, 5.40; N, 9.10.

(*2Z)-2-({(E}[4-Chlorophenylamino]phenylmethylene}hydrazono)-1,4-diphenylbutan-1,4-dione* **(6d):** Pale yellow crystals (0.36 g, 75%); R_f = 0.25 (CH_2Cl_2), m.p. 172°C (ethanol). IR (KBr): ν = 3230 (m, NH), 3060–3010 (m, Ar-CH), 1706–1690 (s, C=O), 1618, 1612 (s, C=N), 1598 (s, C=C) cm^{-1}. UV (CH_3CN): λ_{max} (log ε) = 398 (3.8). ^1H NMR ($CDCl_3$): δ = 8.18 (s, 1H, NH), 8.00–7.96 (m, 2H, ArH), 7.60–7.36 (m, 7H, ArH), 7.26–7.10 (m, 6H, ArH), 6.90–6.86 (m, 2H, ArH), 6.70 (d, 2H, *J* = 8.0 Hz, ArH), 4.68 (s, 2H, CH_2-benzoyl). ^{13}C NMR ($CDCl_3$): δ = 196.0, 193.2 (*C*O), 160.0, 157.4 (*C*=*N*), 140.0 (*N*-Ph *C*), 138.0, 137.8, 137.5 (Ph *C*), 134.0 (Cl-Ph *C*), 128.0, 127.6, 127.2 (Ar *o*-2*C*H), 127.0, 126.8, 126.6, 126.4 (Ar *m*-2*C*H), 125.8, 125.6, 125.2 (Ar *p*-*C*H), 124.5 (Cl-Ph 2*C*H), 37.6 (*C*H_2-benzoyl). MS (EI, 70 eV): *m/z* (%) = 481 [M + 2] (32), 479 [M^+] (100), 477 (26), 251 (54), 248 (56), 233 (22), 231 (20), 128 (23), 126 (26), 118 (38), 107 (72), 105 (76), 77 (36). $C_{29}H_{22}ClN_3O_2$ (479.97): Calcd. C, 72.57; H, 4.62; Cl, 7.39; N, 8.75. Found: C, 72.40; H, 4.68; Cl, 7.35; N, 8.66.

(*2Z)-2-({(E}[3-Chlorophenylamino]phenylmethylene}hydrazono)-1,4-diphenylbutan-1,4-dione* **(6e):** Pale yellow crystals (0.34 g, 70%); R_f = 0.25 (CH_2Cl_2), m.p. 210–212°C (ethanol). IR (KBr): ν = 3220 (m, NH), 3060–3010 (m, Ar-CH), 1708–1686 (s, C=O), 1610, 1608 (s, C=N), 1598 (m, C=C) cm^{-1}. UV (CH_3CN): λ_{max} (log ε) = 390 (3.6). ^1H NMR ($CDCl_3$): δ = 8.20 (s, 1H, NH), 8.00–7.97 (m, 2H, ArH), 7.60–7.30 (m, 9H, ArH), 7.24–7.16 (m, 5H, ArH), 6.80–6.76 (m, 2H, ArH), 6.72 (d, 1H, *J* = 1.3 Hz, ArH), 4.68 (s, 2H, CH_2-benzoyl). ^{13}C NMR ($CDCl_3$): δ = 196.2, 194.0 (*C*O), 160.2, 157.6 (*C*=*N*), 140.4 (*N*-Ph *C*), 138.2, 138.0, 137.8 (Ph *C*), 133.2 (Cl-Ph *C*), 128.0, 127.6, 127.4 (Ar *o*-2*C*H), 127.2, 127.0, 126.8, 126.6 (Ar *m*-2*C*H), 126.0, 125.8, 125.4 (Ar *p*-*C*H), 122.2 (Cl-Ph *o*-2*C*H), 37.4 (*C*H_2-benzoyl). MS (EI, 70 eV): *m/z* (%) = 481 [M + 2] (30), 479 [M^+] (100), 477 (28), 251 (56), 248 (60), 233 (24), 231 (24), 128 (14), 126 (18), 118 (40), 107 (75), 105 (78), 77 (32). $C_{29}H_{22}ClN_3O_2$ (479.97): Calcd. C, 72.57; H, 4.62; Cl, 7.39; N, 8.75. Found: C, 72.50; H, 4.60; Cl, 7.30; N, 8.70.

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